Therapeutic apheresis in exogenous poisoning and in myeloma

D. St. Nenov and K. Sv. Nenov

Medical University of Varna, Bulgaria

Introduction

Plasmapheresis (PF) has been utilized in the treatment of a large variety of more than 150 different disease entities. Its efficacy has not been proven to date in many of them, but its use has been reasoned by attempts to remove circulating humoral factors such as immune complexes, autoantibodies, immunoglobulins, mediators of inflammation, and other endogenous and exogenous toxins [1,2]. Such humoral factors are pathogenetically involved in glomerulonephritis with deposition of antibodies or circulating immune complexes, and in a variety of autoimmune diseases with production of autoantibodies or immune complexes [3]. The effect of plasmapheresis upon the immune system was compared in the past as one of an ‘artificial reticulo-endothelial system’, in analogy with the role of haemodialysis as an artificial kidney. PF has also proven to be of significant benefit in the treatment of certain exogenous intoxications. In patients with phalloid mushroom intoxications, PF is capable of removing the exogenous toxin and can be life-saving when instituted early.

Various methods of plasma separation have emerged since plasma removal with or without substitution has been used as a therapeutic modality. These include plasma filtration and discontinuous and continuous plasma centrifugation. In addition, various methods of plasma treatment without plasma removal, but aimed at removal of certain plasma constituents after plasma separation with subsequent return of treated plasma, have been successfully applied. The latter include cryofiltration, immunoabsorption, LDL-apheresis and chemical affinity column pheresis. Plasma exchange with a centrifugal plasma separator has been reported to be the most widely used modality of plasmapheresis in the USA [4].

Plasma exchange in myeloma nephropathy

Removal of plasma from patients with myeloma has been utilized to treat the associated hyperviscosity syndrome as well as to decrease the plasma level of myeloma paraprotein and in this way to reduce its toxic effects on the kidneys [5,6]. In order to decrease plasma viscosity some authors have advocated that only electrolyte solutions should be used as replacement solutions when the patient’s plasma is being removed in quantity of less than 1.5 l per week [7]. Such a treatment would be expected to continue for months to years to maintain the long-term effects on plasma viscosity. While hyperviscosity is a consequence of very high concentrations of myeloma paraproteins, the latter are also harmful because they can be nephrotoxic. In addition, IL-6 has been involved in the pathogenesis of multiple myeloma, which is another potential therapeutic target for plasmapheresis [8].

Myeloma is only one disease entity of a number of diseases comprising the group of paraproteinemias. Other diseases caused by or associated with paraproteins are Waldenstrom’s macroglobulinaemia, light chain disease, monoclonal gammopathy, hyperviscosity syndrome, amyloidosis, and cryoglobulinaemia. Some of these diseases may be interrelated and may be associated with one another [4]. PF has been experimented as a treatment modality in some of them and has been successfully used in patients with cryoglobulinaemia.

Materials and methods

Thirty-seven patients with myeloma nephropathy were treated with plasmapheresis for a period of several months up to 3 years. In all patients the diagnosis of multiple myeloma was established by bone marrow biopsy and immunohistochemistry. Plasma exchange was performed using a Haemonetics® discontinuous flow cell separator. A mean of 2 l of plasma were exchanged during each treatment session. Twice or even once a week plasma exchanges were performed, the latter regimen being applied when treatment was continued for more than several months. Three daily or every-other-day plasma exchanges were performed initially.

Correspondence and offprint requests to: D. St. Nenov, Clinic of Nephrology, Hemodialysis and Toxicology, Medical University of Varna, 55 M. Drinov St., 9002 Varna, Bulgaria.

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in patients with associated hyperviscosity syndrome. Cytostatic treatment was then instituted. Total plasma protein, fibrinogen, blood viscosity and phagocytic activity were followed monthly.

Results

Clinical improvement was observed after treatment with plasmapheresis for 9–63 months [9,10]. Disappearance of proteinuria was observed in some patients and served as a good prognostic parameter of slowing the progression of myeloma nephropathy.

After plasmapheresis, total plasma protein decreased from 99.4 ± 4.3 to 72.9 ± 4.3 g/l after plasma exchange ($P < 0.01$). Blood viscosity also significantly decreased from 4.6 ± 0.2 to 3.7 ± 0.1 cps ($P < 0.05$). Significant improvement of the phagocytic activity of peripheral polymorphonuclear leucocytes was observed from 25.9 ± 2.0 to 41.0 ± 3.2% spontaneously phagocytesing cells in cell culture ($P < 0.05$). Plasma fibrinogen was numerically, but not significantly reduced from 2.43 ± 0.36 to 1.94 ± 0.31 g/l after plasma exchange ($P = $N.S.). There was no change in plasma osmolality.

Plasmapheresis in phalloid mushroom poisoning

Phalloid mushroom intoxication is a life-threatening condition, which is associated with severe gastrointestinal distress, frequently followed by acute hepatic failure and fatal outcome. The amanita toxin cannot be removed by haemodialysis and is rapidly deposited in the liver, where it exerts its most deleterious effects. Therefore, besides prompt gastrointestinal lavage, extracorporal methods to remove the exogenous toxin are the mainstay in the treatment of phalloid mushroom intoxication and should be performed within the first 12–24 h following ingestion of the poison. PF is an effective treatment and must be performed as soon as the diagnosis is supported by the patient's history, clinical presentation or elevated transaminases [11–14]. In several series, treatment with PF was able to decrease the mortality from phalloid mushroom poisoning from nearly 50 to 10–15% [12]. The residual mortality was due to late arrival or late diagnosis of the patient and subsequent late institution of extracorporal treatment.

We treated eight patients with *Amanita phalloides* poisoning with three to four daily plasma exchanges with removal of at least 2.5 l of patient’s plasma and substitution with donor plasma. Four patients arrived late for treatment, 36–72 h after ingestion of the mushroom, and had a fatal outcome. The other four patients arrived earlier, 16–24 h after ingestion of the poison. Three of them responded well to PF and survived this otherwise fatal intoxication.

While no uniform guidelines for the use of PF in phalloid intoxication have been established, early diagnosis, early institution of treatment and strict adherence to prompt gastrointestinal decontamination are the mainstay in the treatment of this serious condition.

Conclusion

PF has emerged as an important part in the treatment of a great variety of mostly autoimmune diseases. However, PF can be a major therapeutic modality in a number of other disorders, such as multiple myeloma and in different exogenous intoxications. In patients with myeloma, PF is able to improve the hyperviscosity syndrome and possibly to slow down the progression of myeloma nephropathy. In patients with exogenous intoxications it is a key therapeutic modality whenever the poisonous substance is in the patient’s plasma, but cannot be removed by other methods such as haemodialysis.

References

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